UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,276	11/18/2005	Thomas Wisniewski	05986/100M536-US1	3691

7278 7590 08/07/2008

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
08/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/558,276	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-13,15-20,23,28-31,33-37,40,45 and 46* is/are pending in the application.

4a) Of the above claim(s) *11-13,15-19,29-31,33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 9, 10, 20, 22, 28, 45 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed April 28, 2008 in response to the Office Action of December 28, 2007 is acknowledged and has been entered. Claims 2, 5-8, 14, 21, 24-27, 32, 38, 39, 41-44 and 47-50 have been canceled. Rejections of record of canceled claims are moot. Claims 1, 3, 12, 20, 22, and 45 have been amended. Claims 11-13, 15-19, 29-31, 33-37 and 40 are withdrawn. Claims 1, 3, 4, 9, 10, 20, 22, 23, 28, 45 and 46 are under examination in this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 1-4, 9, 10, 20-23, 28, 38, 39, 45, and 46 are rejected under 35 U.S.C. 112, first paragraph, **is withdrawn** in view of Applicant's amendment.

Rejection of claim 28 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is maintained.** It is apparent that the *Salmonella* spp strains, *Salmonella typhimurium* LVR01, LVR03, and SL3261, *Salmonella enteritidis* LVR02, and *Salmonella typhi* CVD915 are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be

satisfied by a deposit of the *Salmonella typhimurium* LVR01, LVR03, and SL3261, *Salmonella enteritidis* LVR02, and *Salmonella typhi* CVD915 strains. See 37 CFR 1.802.

Applicants request that rejection be held in abeyance until one or more claims are found to be allowable.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 3 and 9 under 35 U.S.C. 102(e) as being anticipated by Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) **is withdrawn** in view of Applicant's amendment.

Claim Rejections - 35 USC § 103

Rejection of claim 4 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) as applied to claims 1-3 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's amendment.

Rejection of claims 9 and 10 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is withdrawn** in view of Applicant's amendment.

Rejection of claims 20, 22, 28 and 45 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Lu et al. (US

Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's amendment.

Rejection of claims 23 and 46 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Lu et al. (US Patent 5,733,760) as applied to claims 22 and 45 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) **is withdrawn** in view of Applicant's amendment.

New rejections in view of Applicant's amendment

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1).

Claims are drawn to a vaccine and a pharmaceutical composition comprising a mammalian prion protein and an adjuvant eliciting a humoral immune response. The prion protein comprises an amino acid sequence which is a member of the group consisting of residues 93-156 or residues 123-225 of SEQ ID NO: 4. The adjuvant is aluminium hydroxide. The composition comprises alum as a pharmaceutically acceptable excipient. The composition is

suitable for mucosal administration and elicits a humoral immune response that is predominantly associated with a IgA response when administered to mucosal immune system.

It is noted the claims recite an open language with regard to the sequences represented by residues 93-156 and 123-225 of the SEQ ID NO: 4. Therefore the claims are anticipated by a full length SEQ ID NO: 4 comprising residues 93-156 and 123-225. It is also noted that elected SEQ ID NO: 4 represents elk prion protein (see specification page 4).

Bachman et al. teach a composition comprising a mammalian prion protein, wherein the prion protein sequence is identical with the presently claimed SEQ ID NO: 4 and represents the elk prion protein (see SEQ ID NO: 82 of the sequence listing, and claims 1, 14, and 15). Bachman et al. disclose compositions comprising mammalian prion proteins formulated with an adjuvant aluminium hydroxide eliciting humoral immune response and alum as a pharmaceutically acceptable excipient –an antigen carrier (see [0035], [0080], and Example 15).

Bachman does not teach a composition is suitable for mucosal administration and elicits a humoral immune response that is predominantly associated with an IgA response when administered to mucosal immune system.

Gizurarson et al. teach compositions comprising prion proteins suitable for mucosal administration (see claims 1-28 and columns 2-6). Gizurarson teaches that his compositions formulated for mucosal administration provide enhanced adhesion of the antigen to the mucosal membrane and enhance absorption of the antigen through the mucus membrane, and that the mucosal administration provides the ability to elicit both a systemic (e.g., antibodies of the IgG isotype) and a local (e.g., secretory antibodies of the IgA isotype) immune response in the

recipients of the composition without causing unacceptable irritation of the epithelial membrane (see column 2, lines 48-65).

It would have been obvious to provide Bachman's composition comprising prion proteins for mucosal administration as taught by Gizurarson.

One would have been motivated to provide Bachman's composition formulated for mucosal administration because Gizurarson teaches that his compositions formulated for mucosal administration provide enhanced adhesion of the antigen to the mucosal membrane and enhance absorption of the antigen through the mucus membrane, and that the mucosal administration provides the ability to elicit both a systemic (e.g., antibodies of the IgG isotype) and a local (e.g., secretory antibodies of the IgA isotype) immune response in the recipients of the composition without causing unacceptable irritation of the epithelial membrane (see column 2, lines 48-65).

One would have had a reasonable expectation of success to provide prion composition for mucosal administration because the guidance for providing such compositions is available in the art.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1) as applied to claim 1 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005).

Claim is drawn to the composition comprising a mammalian prion protein wherein all amino acids of the prion protein are D-amino acids.

Bachman et al. and Gizurarson et al. teach a composition comprising a mammalian prion protein for mucosal administration, wherein the prion protein sequence is identical with the presently claimed SEQ ID NO: 4 and represents the elk prion protein (see SEQ ID NO: 82 of the sequence listing, and claims 1, 14, and 15), as discussed above. Neither Bachman et al. nor Gizurarson et al. teach the prion protein wherein all amino acids are D-amino acids.

Benkirane et al. teach that changing the amino acids within an antigenic peptide from an L-residue to the corresponding D-residue drastically increases the antigenicity of the peptide and contributes to the generation of high levels of IgG3 antibodies in immunized animals (see the entire document, particularly page 26279 and Discussion).

Thus based on the teaching of Benkirane et al., it would have been *prima facie* obvious to the person skilled in the art to provide a pharmaceutical composition designed for induction of immune responses, wherein the amino acids within the antigenic protein are D-amino acids.

One would have been motivated to provide Bachman's pharmaceutical composition comprising mammalian prion protein wherein the amino acids of the prion protein are D-amino acids, because Benkrine et al. teach that changing the amino acids within an antigenic peptide from L- to D- amino acids results in increased antigenicity and thus better immunogenicity of the peptide.

One would have had a reasonable expectation of success to provide a composition comprising a mammalian prion protein wherein all amino acids are D-amino acids, because the means required for the synthesis of proteins containing D-amino acid residues have been

available to the skilled artisan at the time of the present invention as evidenced by Benkriane et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1)as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1).

Claims are drawn to the composition comprising a mammalian prion protein wherein the prion protein is covalently attached to the cholera toxin subunit B.

Bachman et al. and Gizurarson et al. teach compositions comprising a mammalian prion protein for mucosal administration, as discussed above. Neither Bachman et al. nor Gizurarson et al. teach the composition wherein the prion protein is covalently attached to the cholera toxin subunit B.

Clemens et al. teach cholera toxin subunit B as an effective adjuvant comprised in vaccine compositions comprising viral or bacterial antigens (see the entire document, particularly claims 1-7 and column 4, lines 28-51). It is noted that Clemens et al. also teach another adjuvant species recited in claim 9, the heat-liable enterotoxin (LT) (see column 9, lines 60-67 and column 10, lines 1-67). Clemens et al. do not expressly teach covalent attachment of cholera toxin subunit B to the antigenic protein. Kleanthous et al. teach covalent attachment of cholera toxin subunit B adjuvant to the antigenic protein (column 5, lines 1-20).

It would have been *prima facie* obvious to covalently attach cholera toxin subunit B to the prion protein. One would have been motivated to covalently attach Clemens' cholera toxin subunit B to Bachman's prion protein, because Clemens' teach that cholera toxin subunit B adjuvant allows for improved mode of oral immunization and development of serum and mucosal antibodies against pathogenic microorganisms and that the cholera toxin subunit B is useful in combination with any specific antigen where a specific neutralizing antibody response would be beneficial in ablating the disease state associated with the antigen (see column 9, lines 5-26).

One would have had a reasonable expectation of success to provide a pharmaceutical composition comprising prion protein covalently attached to the cholera toxin subunit B, because a covalent attachment of cholera toxin subunit B to antigens of interest has been successfully practiced in the art as evidenced by Kleanthous et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 20, 22, 28 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005).

Claims are drawn to a vaccine composition comprising an attenuated *Salmonella typhi* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein, wherein the prion protein comprises an amino acid sequence which is a member of

the group consisting of residues 93-156 or residues 123-225 of SEQ ID NO: 4. The Salmonella strain is *Salmonella typhimurium* LVR01.

It is noted the claims recite an open language with regard to the sequences represented by residues 93-156 and 123-225 of the SEQ ID NO: 4. Therefore the claims are anticipated by a full length SEQ ID NO: 4 comprising residues 93-156 and 123-225. It is also noted that elected SEQ ID NO: 4 represents elk prion protein (see specification page 4).

Bachman et al. and Gizurarson et al. teach composition comprising a mammalian prion protein formulated for mucosal administration as discussed above, wherein the prion protein sequence is identical with the presently claimed SEQ ID NO: 4 and represents the elk prion protein (see SEQ ID NO: 82 of the sequence listing, and claims 1, 14, and 15). Bachman's prion protein is comprised within the viral like particle and not the attenuated *Salmonella typhi* bacterium transfected spp strain as required by the present claims.

Lu et al. teach vaccine compositions comprising attenuated *Salmonella* vectors expressing heterologous DNA encoding viral antigens from HIV and HCV viruses (see the entire document, particularly claims 1-9, column 5, lines 65-67, column 10, lines 19-60). While Lu et al. teach *Salmonella typhi, Salmonella typhimurium, and Salmonella enteritidis*, (see column 6, lines 65-67, Lu et al. does not teach the specific *Salmonella* strains as recited in the present claim 28.

Chabalgoity et al. teach *Salmonella typhimurium* LVR01 strain expressing heterologous antigens encoding binding fatty acid protein from *Echinococcus granulosus* (see the entire document, particularly Materials and Methods).

It would have been *prima facie* obvious to express mammalian prion protein in *Salmonella* bacterial vectors used for expression of heterologous antigens. Therefore it would have been obvious to provide a composition comprising attenuated *Salmonella typhi* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein.

One would have been motivated to substitute Lu's attenuated *Salmonella* vectors for Bachman's viral particles and express mammalian prion proteins in *Salmonella* vectors because Lu et al. teach that their *Salmonella* vectors are particularly effective for induction of mucosal protective immune responses against mucosally transmitted infectious agents. Lu et al. also teach that attenuated Salmonella vectors are effective vectors for delivery of desired antigens because the bacteria grow rapidly and do not require growth in cell culture, thus allowing large scale production of vectors (see column 1, lines 19-55).

One would have been motivated to use Chabalgoity's *Salmonella typhimurium* LVR01 strain for expression of Bachman's prion proteins because Chabalgoity et al. teach that heterologous antigens expressed in LVR01 effectively elicits humoral and cellular immune responses in animals (see the entire document, particularly Results and Discussion on page 468).

One would have had a reasonable expectation of success to provide a composition comprising an attenuated *Salmonella typhi* bacterium and particularly *Salmonella typhimurium* LVR01 transformed with a vector capable of expressing a mammalian prion protein because the technology used for generation of bacterial recombinant vectors has been available to the skilled artisan at the time of the present invention. Moreover, the bacterial recombinant vectors

expressing heterologous antigens have been successfully made in the art at the time of the invention as evidenced by Lu et al. and Chabalgoity et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 23 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) as applied to claims 22 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285).

Claims are drawn to a vaccine composition comprising an attenuated *Salmonella typhii* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein, wherein all amino acids of the prion protein are D-amino acids.

Bachman et al. Gizurarson et al. and Lu et al. teach a vaccine composition comprising an attenuated *Salmonella typhii* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein as discussed above.

Benkirane et al. teach that changing the amino acids within an antigenic peptide from an L-residue to the corresponding D-residue drastically increases the antigenicity of the peptide and contributes to the generation of high levels of IgG3 antibodies in immunized animals (see the entire document, particularly page 26279 and Discussion).

Thus based on the teaching of Benkirane et al., it would have been *prima facie* obvious to the person skilled in the art to provide a pharmaceutical composition designed for induction of immune responses, wherein the amino acids within the antigenic protein are D-amino acids.

One would have been motivated to provide Bachman's and Lu's pharmaceutical composition comprising attenuated *Salmonella typhii* transformed with a vector capable of expressing a mammalian prion protein wherein the amino acids of the prion protein are D-amino acids, because Benkirane et al. teach that changing the amino acids within an antigenic peptide from L- to D- amino acids results in increased antigenicity of the peptide.

One would have had a reasonable expectation of success to provide a composition comprising a mammalian prion protein wherein all amino acids are D-amino acids and to successfully use this composition for immunization purposes, because the means required for the synthesis of proteins containing D-amino acid residues have been available to the skilled artisan at the time of the present invention as evidenced by Benkirane et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground of rejections presented in this Office action. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen, Ph.D./
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648